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Comparison of Corneal Biomechanical Properties between Indian and Chinese Adults

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Purpose: To investigate the difference in corneal hysteresis (CH) and corneal resistance factor (CRF) between Indian and Chinese populations.

Design: Population-based cross-sectional study.

Participants: Three hundred eighty-two Singaporean Indian persons and 764 Singaporean Chinese 50 years of age or older were included from the Singapore Indian Eye Study and Singapore Chinese Eye Study, respectively.

Methods: Participants underwent standardized systemic and ocular examinations and interviewer-administered questionnaires for risk factor assessment. The CH and CRF were measured with the Ocular Response Analyzer (Reichert Ophthalmic Instruments, Buffalo, NY). Information on genetic ancestry was derived using principal component analysis. Linear regression models were used to investigate the association of CH and CRF with potential risk factors.

Main Outcome Measures: Corneal hysteresis and CRF.

Results: After excluding participants with a history of intraocular surgery, a diagnosis of glaucoma suspect or glaucoma, refractive surgery, or presence of corneal abnormalities, CH and CRF readings were available for 382 Indian persons. For each Indian participant, 2 Chinese participants were selected and matched for age and gender (n = 764). There were no differences in the clinical measurements of CH (10.6±1.6 mmHg; $P = 0.670$) or CRF (10.3±1.7 mmHg; $P = 0.103$) between the ethnic groups. However, after adjusting for covariates, Indian persons had, on average, 0.18-mmHg higher CH levels than in Chinese (95% confidence interval [CI], 0.02−0.38; $P = 0.031$). Consistently, CH level was correlated significantly with genetic ancestry in the Southeast Asian population. Corneal resistance factor level was not associated independently with self-reported ethnicity (95% CI, −0.10 to 0.29; $P = 0.335$).

Conclusions: Chinese have lower CH than Indian persons, and this disparity may reflect biomechanical differences of the cornea. *Ophthalmology 2017;■:1−9 © 2017 by the American Academy of Ophthalmology*

Glaucoma is the second leading cause of irreversible blindness worldwide.[1,2] Increasing evidence suggests that conventional anatomic risk factors for primary open-angle glaucoma (POAG) do not explain adequately why many people with elevated intraocular pressure (IOP) and thin central corneal thickness (CCT) never demonstrate the disease. Clear evidence for the failure of IOP and CCT to explain the disease is the fact that Chinese persons have a reduced glaucoma-related risk profile (lower IOP and thicker cornea) than Indian persons,[3] yet our population-based data show no reduced POAG prevalence among a Chinese population compared with an Indian population.[4,5] If Chinese persons have a reduced glaucoma-related risk profile (lower IOP and thicker cornea) than Indian persons, then something other than IOP and CCT must explain their similarly high glaucoma prevalence as that of Indian persons. Thus, deciphering why certain individuals are susceptible to glaucoma may reside in other properties of the eye, and not simply in the IOP or CCT.

Corneal hysteresis (CH) and corneal resistance factor (CRF) are clinical measurements of corneal biomechanics that can be measured from the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY).[6−8] It has been speculated that corneal biomechanical properties may reflect that of the sclera and optic nerve head. Low CH, representing a less viscoelastic cornea, seems to be an indicator of which eyes will demonstrate POAG.[9−11] In light of its relevance to glaucoma, a comparison of the CH and CRF values between Indian and Chinese persons, the 2 largest racial and ethnic groups globally, may provide useful clinical information for glaucoma assessment for different ethnic groups.[4,5] However, such direct comparisons using similar examination protocols across ethnic groups have not been performed. The purpose of the current study was to examine variations of CH and CRF between Chinese and Indian persons living in Singapore. We hypothesized that despite having lower IOP and thicker CCT, Chinese people may have POAG prevalence as high as that of Indian persons as a result of lower CH.

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Methods

Study Population

Participants in this study were derived from Chinese and Indian persons who participated in a substudy under the Singapore Epidemiology of Eye Disease study. Chinese participants were from the Singapore Chinese Eye Study (2009−2011), whereas Indian persons were from the Singapore Indian Eye Study (2012−2015). In brief, an age-stratified (by 10-year age groups) random sampling in each ethnic group was used to select ethnic Indian and Chinese persons 40 to 80 years of age living across the southwestern part of Singapore during each stipulated study period. Study methodology and details were identical and have been described elsewhere.[12] In brief, the Singapore Epidemiology of Eye Disease study is an ongoing, population-based study that was designed to evaluate the prevalence, risk factors, and impact of major eye diseases among Singaporeans 40 to 80 years of age residing in the southwestern part of Singapore.

For this substudy, 551 consecutive Indian participants who attended the study clinic during their follow-up examination between April 1 and August 31, 2015, were included. Of the 551 recruited Indian participants, 169 participants were excluded because of a history of intraocular surgery (n = 95) or because of being glaucoma suspects or being diagnosed with glaucoma (n = 74). Finally, 382 Indian participants (69.3%) were included in the analysis.

A total of 3353 Chinese persons participated in the study between 2009 and 2011. Among these, 2878 (86.8%) underwent corneal biomechanical measurement, after excluding those with missing corneal biomechanical measurements (n = 43), history of intraocular surgery (n = 341), and glaucoma suspects or those with glaucoma (n = 91). We previously published the corneal biomechanical profile of the Chinese population showing that age and gender were determinants for CH and CRF.[13] Therefore, we applied a frequency-matching technique based on age (by 5-year age groups) and gender matching, whereby 2 Chinese participants were selected for each Indian participant. Therefore, 764 age- and gender-matched Chinese participants were selected randomly from those Chinese participants with available corneal biomechanical measurements (n = 2878). Ethics approval was obtained from the Singapore Eye Research Institute Institutional Review Board. All study participants provided written informed consent in adherence to the tenets of the Declaration of Helsinki.

Examination Procedures

Both Indian and Chinese participants underwent similar clinical and ocular examinations in the same clinic (Singapore Eye Research Clinic).[12] Each participant underwent a standardized interview and eye examination that included assessment of best-corrected visual acuity, assessment of corneal biomechanical properties by the ORA, autorefraction, and keratometry (corneal curvature in millimeters; Canon RK-5, Autoref-Keratometer [Canon Inc., Ltd., Ōta, Japan]).[14] Spherical equivalent was defined as sphere plus half cylinder. Ocular biometry, including anterior chamber depth and axial length, was measured using noncontact partial coherence interferometry (IOLMaster; Carl Zeiss Meditec, Dublin, CA), CCT was measured by an ultrasound pachymeter (Advent; Mentor O & O, Inc., Norwell, MA), and IOP was measured by Goldmann applanation tonometry (Haag-Streit, Koenz, Switzerland). Slit-lamp examination of the anterior segment, evaluation of the retina, and dynamic gonioscopy (Sussman 4-mirror gonioscope; Ocular Instruments, Inc., Bellevue, WA) were conducted by the study ophthalmologists.[15] Each participant underwent height and weight measurement, and these were used to determine the body mass index, which was calculated as body weight (in kilograms) divided by body height (in meters) squared. Seated blood pressure and blood samples were collected during the examination procedures. Hypertension was defined as systolic blood pressure of 140 mmHg or more, diastolic blood pressure of 90 mmHg or more, physician diagnosed hypertension, or self-reported history of hypertension. Diabetes mellitus was defined as random glucose of 11.1 mmol/l or more, diabetic medication use, or a physician-diagnosed history of diabetes.

Ocular Response Analyzer

Details regarding the ORA have been published previously.[16] The ORA uses a noncontact rapid air pulse to generate a signal. The ORA signal depicts 2 IOP measurements. The difference between the first and second measurement is the CH and is an indicator of the viscous properties of the cornea. The ORA also provides measurement of CRF, which is an indicator of the overall resistance or elastic properties of the cornea.[17]

The ORA parameters were measured in the right eye of each eligible participant; when the right eye was ineligible, parameters were measured in the left eye. The measurement was repeated 3 times; differences between the ORA pressure readings of more than 3 mmHg warranted a fourth measurement. Exclusion criteria for this analysis were a history of intraocular surgery or refractive surgery, presence of corneal abnormalities such as keratoconus, corneal scarring that would preclude accurate ORA and IOP measurements, or a diagnosis of glaucoma suspect or glaucoma. Glaucoma suspects were defined according to prespecified criteria,[15,18] which included IOP of more than 21 mmHg, gonioscopic findings of occludable angles, presence of peripheral anterior synechiae, cup-to-disc ratio of more than 0.6, disc asymmetry with cup-to-disc ratio difference of more than 0.2, pseudoexfoliation syndrome, pigment dispersion syndrome, and known glaucoma patients. Glaucoma was diagnosed according to the International Society of Geographical and Epidemiologic Ophthalmology classification.[18]

Ancestry Inference Using Genome-Wide Single Nucleotide Polymorphism Markers

In addition to self-reported ethnicity, individual genetic ancestry were inferred using principal component (PC) analysis by the smartPCA program (EIGENSTRAT software version 4.2)[19] to examine the relationship of race and its associations to CH and CRF.[20] The method implemented in EIGENSTRAT works well if markers are independent[21]; hence, PC analysis was applied to a reduced single nucleotide polymorphism (SNP) set that had low linkage disequilibrium. The following steps were taken to arrive at a final set of 57 237 SNPs. Autosomal SNPs with minor allele frequency of 0.05 or more within each ethnic group in our study population were selected and used for analysis. Genotype data, which had undergone strict quality checks, were merged together and only SNPs shared by both ethnic groups were used for analysis. In addition, known high linkage disequilibrium regions were excluded (Chr5, 44−51.5 Mb; Chr6, 25−37 Mb; Chr8, 1−12.7 Mb; Chr11, 45−57 Mb; and Chr11, 84−86 Mb).[22] Then, SNPs were pruned using the indep-pairwise option in PLINK (version 1.07; available at: http://pngu.mgh.harvard.edu/~purcell/plink/; accessed September 1, 2016.), with a window size of 50 SNPs, shifting by 5 SNPs at each step and removing 1 of a pair of SNPs if the linkage disequilibrium was more than 0.2. We then applied PC analysis to genotype data to infer continuous axes of genetic variation. Intuitively, the axes of variation reduce the data to a small number of dimensions,